REMARKS

Claims 1, 3-8, 10-17 and 19-24 are pending in the application. Claims 3 and 23 have been amended to address the Examiner's section 112 rejections.

Claims 1, 3-8, 10-17 and 19-24 have been rejected under 35 USC.§103(a) as allegedly unpatentable over Hoofnagle in view of Huang et al and Mutchnick. Applicants respectfully traverse this rejection.

The present invention is directed to a composition for treating Hepatitis C that contains α-interferon and thymosin. More specifically, the composition is a pharmaceutical dosage unit of a pharmaceutically acceptable carrier containing an immune system-potentiating amount of at least one member selected from the group consisting of thymosin and immune system-potentiating fragments of thymosin in combination with an anti-hepatitis C viral effective amount of at least one α-interferon. The pharmaceutical dosage unit is capable of promoting *in vivo* inactivation of hepatitis C virus when administered to mammals infected with said virus.

None of the cited references, whether taken alone or in combination suggest the combination of these two ingredients as a suitable and effective means for treating Hepatitis C.

Before the references are discussed, it is important to understand that Hepatitis C is caused by an RNA virus. On the other hand, Hepatitis B is caused by a DNA virus. These two types of viruses operate differently in a host. For Hepatitis C, the injury is mostly caused by the virus itself. For Hepatitis B, the injury is caused by the immunologic response to the virus. Therefore, no generalized assumption would have been made by one of ordinary skill in the art that a therapy that works for Hepatitis B would work for Hepatitis C.

Hoofnagle et al. discloses a composition containing α-interferon for treating Hepatitis C. There is no mention of the combination of α-interferon with thymosin. There is also not suggestion of what the proper dosage unit would be or what parameters would be useful to achieve the proper dosage unit for a Hepatitis C therapy containing α-interferon and thymosin.

Huang et al. is directed to a composition for treating Hepatitis B rather than Hepatitis C. Huang et al. combines interferon and thymosin to treat Hepatitis B. Huang is silent about Hepatitis C. Huang et al also does not disclose what type of interferon is used. Specifically, Huang et al. does not disclose the use of α-interferon. The present composition claims require "an anti-Hepatitis C viral effective amount of at least one α-interferon, said pharmaceutical dosage unit being capable of promoting *in vivo* inactivation of hepatitis C virus." The present method claims call for treating Hepatitis C by administering to a mammal an anti-hepatitis C viral effective amount of at least one α-interferon, concurrently or consequentially with administering a thymosin or thymosin fragment. Huang et al does not make up for the deficiency in Hoofnagle, because Huang does not indicate that thymosin is useful for treating Hepatatic C.

Mutchnick, et al. (1991) discloses the use of Thymosin fraction 5 to be useful for the treatment of Hepatitis B. Although the article may indicate that thymosin fraction 5 has been shown to trigger maturational events in lymphocytes, to augment T cell function and promote reconstitution of immune defects, the article only states, "These thymosins may provide an alternative approach to the treatment of chronic HBV infection." The article is not conclusive regarding the benefit for Hepatitis B. Moreover, it is silent regarding the benefits of thymosin on Hepatitis C, a totally different virus with different genetic make-up.

It is impossible from reading Mutchnick, et al to know if thymosin would be useful for treating Hepatitis C any more than it could be said that it would help AIDS, Herpes or any other viral infections. The diseases are not the same.

Further, there is no suggestion in any of the references that a pharmaceutical formulation for Hepatitis B would work for Hepatitis C. In fact, many Hepatitis B specific therapies have no effect on Hepatitis C. For example, Laminvadine® or Adefobir® are Hepatitis B treatments that have no effect on Hepatitis C virus. Therefore, it is not obvious to one of ordinary skill in the art that an agent that works for one virus will automatically work for the other virus. Since none of the references, whether taken alone or in combination, indicate how to modify Huang, et al. to arrive at a formulation that meets the language in the claims, one of ordinary skill in the art would not have been led to the present invention.

Enclosed, herewith is a 1999 article of Mutchnick, et al. It is not cited as prior art because it postdates the filing of this application. It is only being cited as evidence that at the time of the invention, one of ordinary skill in the art would not have been able to conclude that the thymosin fraction 5 in Mutchnick (1991) was the cause of improvement for Hepatitis B patients. The 1999 article indicates that Mutchnick, et al. discovered no benefit of the use of thymosin α-1 in a larger trial.

The rejection under 35 USC §103(a) is believed overcome. Reconsideration and allowance are respectfully requested.

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1: J Viral Hepat. 1999 Sep;6(5):397-403. Related Articles, L

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Thymosin alpha1 treatment of chronic hepatitis B: results of a phase III multicentre, randomized, double-blind and placebo-controlled study.

Mutchnick MG, Lindsay KL, Schiff ER, Cummings GD, Appelman HD, Peleman RR, Silva M, Roach KC, Simmons F, Milstein S, Gordon SC, Ehrinpreis MN.

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Previous clinical trials have suggested that thymosin alpha1 (Talpha1), an immunomodulatory peptide, may be effective in the treatment of chronic hepatitis B (CHB). The aim of this study was to determine the efficacy of Talpha1 in a multicentre, placebo-controlled and double-blind study of 97 patients with serum hepatitis B virus (HBV) DNA- and hepatitis B e antigen (HBeAg)-positive CHB. Patients who had been hepatitis B surface antigen (HBsAg) positive for at least 12 months entered a 3-month screening period prior to randomization. Forty-nine patients received Talpha1 (1.6 mg) and 48 patients received placebo, twice weekly for 6 months, and were followed-up an additional 6 months. At inclusion, both groups were comparable for age, gender, histological grading, and aminotransferase and HBV DNA levels. A complete response to treatment, defined as a sustained serum HBV DNA-negative status (two negative results at least 3 months apart) during the 12-month study, with negative HBV DNA and HBeAg values at month 12, was seen in seven (14%) patients given Talpha1 and in two (4%) patients treated

with placebo (P = 0.084). Five (10%) patients given Talpha1 and four (8%) patients given placebo exhibited a delayed response (defined as sustained ser HBV DNA negativity achieved after the 12-month study period with negativ HBV DNA and HBeAg values at the last assessment). A total of 12 (25%) patients given Talpha1 and six (13%) patients given placebo showed a sustained loss of HBV DNA with a negative HBeAg value during or followi the 12-month study period (P < 0.11). These results do not confirm observati of treatment efficacy reported in other clinical studies.

Publication Types:

- Clinical Trial
- Clinical Trial, Phase III
- Multicenter Study
- Randomized Controlled Trial

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